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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,098	10/14/2004	Akira Ideno	Q83564	9139

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EXAMINER	
PROUTY, REBECCA E	
ART UNIT	**PAPER NUMBER**
1652	

MAIL DATE	DELIVERY MODE
08/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/511,098	IDENO ET AL.	
	Examiner	Art Unit	
	Rebecca E. Prouty	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33-64* is/are pending in the application.

4a) Of the above claim(s) *38,39,43-52,57 and 58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33-37,40-42, 53-56 and 59-64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 November 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/04, 1/05, 11/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Claims 1-32 have been canceled. Claims 33-64 are at issue and are present for examination.

Applicant's election without traverse of Group A, claims 33-37, 40-42, 53-56 in the reply filed on 5/23/07 is acknowledged.

Claims 38, 39, 43-52 and 57-58 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 5/23/07.

Claims 33,37, 40, 41, and 42 are objected to because of the following informalities: abbreviations should not be used in the claims without at least indicating what the abbreviation is used for at the first occurrence thereof. Appropriate correction is required.

Claim 35 is objected to because of the following informalities: "a first coding region" and "a region having at least one restriction site" should be "the first coding region" and "the region having at least one restriction site" as these elements have been previously defined in the claim, the word "being" should be deleted, and "and is translated in the same reading frame to be a protease digestion site" should be replaced with "encoding a protease digestion site in the same

reading frame as the first and second coding regions." Appropriate correction is required.

Claim 60 is objected to because of the following informalities: "making express the fused protein in a cytoplasm" should be "expressing the fused protein in the cytoplasm". Appropriate correction is required.

Claim 61 is objected to because of the following informalities: "a first coding region" or "a second coding region" should be "the first coding region" or "the second coding region" as these elements have been previously defined in the claim and "a periplasm or a medium" should be "the periplasm or medium". Appropriate correction is required.

Claim 64 is objected to because of the following informalities: "a protease digestion site" should be "the protease digestion site". Appropriate correction is required.

Claims 59-64 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 59 and 62 are indefinite in the recitation "making the expression vector… express the fused protein" as it is unclear what actions this corresponds to. It is suggested that

this be replaced with "culturing a host cell transformed with the expression vector to express the fused protein"

Claim 60 lacks antecedent basis for "the host".

Claim 61 is unclear in the recitation of "providing a sequence transcribed and translated to be a signal sequence at … a 5′ terminus of the second coding region" as the second coding region is fused to the first coding region such that the presence of a signal sequence between the first and second coding regions would not result in transport of the protein across the membrane of the cell.

Claim 63 is indefinite in the recitation "or its analogous compound" as it is unclear what properties compounds "analogous" to juglone must have.

Claims 33-37, 40-42, 53-56, and 59-64 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to a genus of expression vectors comprising a sequence encoding any petidyl-prolyl isomerase (PPIase) having molecular chaperone activity and methods of use

thereof (Claims 33-36, 53-56, and 59-64) or comprising any FKBP-type PPIase having molecular chaperone activity (Claim 37) or any achaebacterial FKBP-type PPIase or short-type FKBP-type PPIase having molecular chaperone activity (Claims 40-42). The specification teaches the structure of only a few representative species of such sequences encoding a PPIase having molecular chaperone activity. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of PPIase and molecular chaperone activity. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 33-37, 40-42, 53-56, and 59-64 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for expression vectors comprising a sequence encoding PPIase from *Methanococcus thermolithotrophicus*, *Thermococcus* sp. KS-1, *Methanococcus jannaschii*, *Methanosarcina mazei*, *Methanosarcina acetivorans*, and *Methanosarcina barkeri* and uses thereof, does not reasonably provide enablement for expression vectors comprising a sequence encoding any PPIase

having molecular chaperone activity and methods of use thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 33-37, 40-42, 53-56, and 59-64 are so broad as to encompass expression vectors comprising a sequence encoding any PPIase having molecular chaperone activity and methods of use thereof (Claims 33-36, 53-56, and 59-64) or comprising any FKBP-type PPIase having molecular chaperone activity (Claim 37) or any achaebacterial FKBP-type PPIase or short-type FKBP-type PPIase having molecular chaperone activity (Claims 40-42). The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of sequences encoding a PPIase necessary for constructing the vectors encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which

the proteins' structure relates to its function. However, in this case the disclosure is limited to the disclosure of some known PPIase genes for use in making the claimed vectors.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass vectors comprising a sequence encoding any PPIase having molecular chaperone activity or comprising any FKBP-type PPIase having molecular chaperone activity or any achaebacterial FKBP-type PPIase or short-type FKBP-type PPIase having molecular chaperone activity because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting molecular chaperone activity activity; (B) the general tolerance of PPIases to modification

and extent of such tolerance; (C) a rational and predictable scheme for modifying any PPIase residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including vectors comprising a sequence encoding any PPIase having molecular chaperone activity or comprising any FKBP-type PPIase having molecular chaperone activity or any achaebacterial FKBP-type PPIase or short-type FKBP-type PPIase having molecular chaperone activity. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of vectors having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 33-37, 40-42, 53-56, and 59-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fersht (WO 00/75346) in view of Furutani et al.

Ferst teaches expression vectors for producing a fusion protein comprising a chaperone polypeptide fused in frame to a protein of interest. Ferst teaches that suitable proteins of interest include antibodies and membrane proteins (see page 14) and that suitable chaperone polypeptide include any polypeptide which possesses the ability to promote the folding of a polypeptide *in vivo* or *in vitro*. Ferst further teaches the inclusion of a suitable restriction site for insertion of the sequence encoding the protein of interest following the chaperone polypeptide (see page 20), sequences encoding a

protease digestion site between the chaperone polypeptide and the protein of interest (see page 15) and inclusion of a signal sequence preceding the chaperone polypeptide encoding region for the secretion of the fusion protein (see page 24). Ferst does not specifically teach the use of a PPIase having molecular chaperone activity including a short-type archaebacterial FKBP-type PPIase having molecular chaperone activity as the polypeptide having chaperone activity.

Furutani et al. teach recombinant production of PPIase from *Methanococcus thermolithotrophicus* and show that this protein has molecular chaperone activity.

Therefore, as the protein disclosed by Furutani et al. has all the properties disclosed by Ferst as being necessary for the first region of the fusion vectors of Ferst, it would have been obvious to one of ordinary skill in the art to select the PPIase of *Methanococcus thermolithotrophicus* for use in the fusion vectors of Ferst.

The reference lined through on applicants PTO-1449 (JP 2003-501064) was not considered as a copy was not submitted.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca E. Prouty whose telephone number is 571-272-0937. The examiner can normally be reached on Tuesday-Friday from 8 AM to 5 PM. The examiner can also be reached on alternate Mondays

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The fax phone number for this Group is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Rebecca Prouty/
Primary Examiner
Art Unit 1652